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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,174	11/14/2001	Mario Anthony Moscarello	2132.024	6896
21917	7590	08/28/2003		
MCRAE & SLAVIN, P.A. 2855 PGA BLVD PALM BEACH GARDENS, FL 33410			EXAMINER COUTNS, GARY W	
			ART UNIT 1641	PAPER NUMBER 10
			DATE MAILED: 08/28/2003	

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/992,174	MOSCARELLO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 03 June 2003.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.
- Disposition of Claims**
- 4) Claim(s) 22-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 22-26 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

The Request for Continued Examination and the amendment filed June 3, 2003 is acknowledged and has been entered.

### ***Information Disclosure Statement***

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is vague and indefinite because it is unclear when the heparin is added to the ELISA (i.e. is heparin added before the sample or to the sample or is heparin added before the addition of a label or after the addition of a label?).

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bloch et al (US Patent 6,183,988) in view of Voumvourakis et al (Detection of anti-MBP in the serum of patients with multiple sclerosis, Greek Microbiology Organization

Newsletter (1992) 37, 666-672) and further in view of Pesce et al (Cationic antigens Problems associated with measurement by ELISA, Journal of Immunological methods, 87 (1986) 21-27).

Bloch et al disclose a diagnostic method for multiple sclerosis, which comprises obtaining biological samples from a mammalian body fluid such as sera, plasma, CSF, or saliva. Bloch et al disclose contacting the sample with at least one protein and the contacting is by an enzyme-linked immunosorbent assay (col 22 line 52 – col 23, line 22). Bloch et al disclose detecting the binding of autoantibodies in the serum sample (col 4, lines 1-21). Bloch et al also disclose comparing the level of at least one autoantibody in the first biological sample is measured or estimated and compared to that in a standard taken from an individual not having the autoimmune disease (second sample (col 22, lines 37-51). Bloch et al disclose the use of a second antibody used for detection. Bloch et al disclose that the identity of this second antibody will depend upon the identity of the mammal for which the biological sample to be tested is derived; for example, if it is a human serum sample, the second antibody will be an anti-human antibody (col 23, lines 17-22).

Bloch et al differ from the instant invention in failing to teach the protein associated with multiple sclerosis as being myelin basic protein. Bloch et al also fail to teach the autoantibody is anti-MBP IgG and IgM isotypes. Bloch et al also fails to teach the utilization of heparin to reduce non-specific charge interactions with MBP.

Voumvourakis et al disclose that multiple sclerosis has been associated with the presence of antibodies against myelin basic protein (cationic protein) (p. 2-3 of

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translation). Voumvourakis et al also disclose determining anti-MBP of the IgG and IgM isotypes. The aim of this study was to investigate anti-MBP in the serum of patients with M.S. since the occurrence of these antibodies in subjects with multiple sclerosis is controversial.

Pesce et al disclose the use of heparin to reduce non-specific charge interactions of cationic proteins that plague the sensitivities of ELISAs. Pesce et al disclose that non-specific reactivity of the cationic protein could almost completely be eliminated by carrying out the antibody-antigen incubation in the presence of heparin (p. 23) and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen (p. 27).

It would have been obvious to one of ordinary skill in the art to substitute myelin basic protein as taught by Voumvourakis et al for the protein of Bloch et al because Voumvourakis et al shows that multiple sclerosis has been associated with the presence antibodies against myelin basic protein. Furthermore, it would have been obvious to one of ordinary skill in the art to determine anti-MBP IgG and IgM as taught by Voumbourakis et al for the method of Bloch et al because Voumbourakis et al teach that the pathogenesis of multiple sclerosis involves antibodies directed against myelin basic protein and that the aim of the study was to investigate anti-MBP in the serum of patients with multiple sclerosis since the occurrence of these antibodies in subjects with multiple sclerosis is controversial.

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It also would have been obvious to one of ordinary skill in the art to incorporate the use of heparin as taught by Pesce et al into the modified method of Bloch et al because Pesce et al shows that non-specific reactivity of the cationic protein (MBP is cationic) can almost completely be eliminated by carrying out the antibody-antigen incubation in the presence of heparin and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen.

### ***Conclusion***

8. No claims are allowed.
9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Groome (Enzyme-linked Immunoassay Asssays of Myelin Basic Protein and Antibodies to Myelin Basic Protein, J. of neurochemistry, 1980, 35 (6) 1409-1417)  
Groome disclose ELISA assays for Myelin Basic Protein and Antibodies to MBP.  
Groome disclose that MBP is cationic.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts  
Examiner  
Art Unit 1641  
August 19, 2003



LONG V. LE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

08/19/03